Claims

- 1. Use of somatostatin or one of its agonist analogues for preparing a medicament intended to regulate the ovarian follicular reserve, and in particular to reduce the depletion of the ovarian follicular reserve over time, in non-menopausal women.
- 5 **2.** Use according to claim 1, characterized in that somatostatin is used for preparing the medicament.
 - **3.** Use according to claim 1, characterized in that a somatostatin agonist analogue is used for preparing of the medicament.
 - **4.** Use according to claim 3, characterized in that the somatostatin agonist analogue is a compound of general formula (I)

cyclo[A - ZZa - (D/L)Trp - Lys -
$$X_1$$
 - X_2] (I)

in which:

10

15

 X_1 is a radical of formula (a) or (b)

R₁ independently representing at each time that it occurs an optionally substituted phenyl radical in which the optional substituents are independently chosen from a halogen atom and the methyl, ethyl, methoxy and ethoxy radicals,

20 R_2 representing $-Z_1$ - CH_2 - R_1 , $-CH_2$ -CO-O- CH_2 - R_1 ,

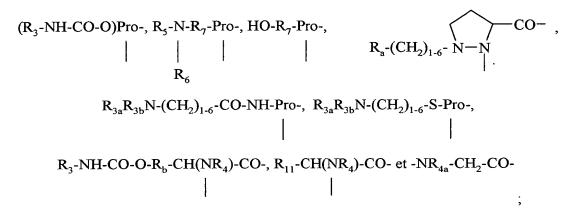
 Z_1 being O or S;

10

15

 X_2 is an α -amino acid having an aromatic residue on the side chain C α , or an amino acid unit chosen from Dab, Dpr, Dpm, His, (Bzl)HyPro, thienyl-Ala, cyclohexyl-Ala and t-butyl-Ala;

5 A is a divalent residue chosen from Pro,



R₃ is NR₈R₉-C₂₋₆alkylene, guanidino-C₂₋₆alkylene or C₂₋₆alkylene-COOH, R_{3a} is H, C₁₋₄alkyl or has, independently, one of the meanings given for R₃, R_{3b} is H or C₁₋₄ alkyl, R_a is OH or NR₅R₆, R_b is -(CH₂)₁₋₃- or -CH(CH₃)-, R₄ is H or CH₃, R_{4a} is benzyl optionally substituted on the aromatic ring, each of R₅ and R₆ is independently H, C₁₋₄alkyl, ω-amino-C₁₋₄alkylene, ω-hydroxy-C₁₋₄alkylene or acyl, R₇ is a direct bond or C₁₋₆alkylene, each of R₈ and R₉ is independently H, C₁₋₄alkyl, ω-hydroxy-C₂₋₄alkylene, acyl or CH₂OH-(CHOH)_c-CH₂- in which c is 0, 1, 2, 3 or 4, or R₈ and R₉ form together with the nitrogen atom to which they are attached a heterocyclic group which can include an additional heteroatom, and R₁₁ is benzyl optionally substituted on the aromatic ring, -(CH₂)₁₋₃-OH, CH₃-CH(OH)- or -(CH₂)₁₋₅-NR₅R₆, and ZZ_a is a natural or unnatural α-amino acid unit;

it being understood that X_1 , X_2 and Lys each have the configuration L;

or is a pharmaceutically acceptable salt or protected form of a compound of general formula (I).

5. Use according to claim 3, characterized in that the somatostatin agonist analogue is a compound of general formula (II)

in which R is $NR_{10}R_{11}$ - C_{2-6} alkylene or guanidine- C_{2-6} alkylene, and each of R_{10} and R_{11} is independently H or C_{1-4} alkyl

(II)

or is a pharmaceutically acceptable salts or a protected form of a compound of general formula (II).

- 6. Use according to claim 3, characterized in that the somatostatin agonist analogue is chosen from the group comprising lanreotide, octreotide, vapreotide, SOM 230, MK-678, BIM-23190, BIM-23197, BIM-23268, PTR-3173, TT-232, the peptide of formula c[Tic-Tyr-DTrp-Lys-Abu-Phe], the KE 108 peptide of formula Tyr⁰-(cyclo-D-Dab-Arg-Phe-Phe-D-Trp-Lys—Thr-Phe) and their pharmaceutically acceptable salts and protected forms.
 - 7. Use according to claim 6, characterized in that the somatostatin agonist analogue is lanreotide or one of its pharmaceutically acceptable salts.
 - **8.** Use according to one of claims 1 to 7, characterized in that the medicament is intended to be administered to a woman at risk of early menopause.
- 9. Use according to one of claims 1 to 7, characterized in that the medicament is intended to be administered to a woman who has an X chromosome microdeletion.
 - 10. Use according to one of claims 1 to 7, characterized in that the medicament is intended to be administered to a woman who has polycystic ovaries.

- 11. Use according to one of claims 1 to 7, characterized in that the medicament is intended to be administered to a woman who is about to have, is currently having or has had chemotherapy or irradiation.
- 12. Use of somatostatin or one of its agonist analogues in toxicology tests relating to another compound in order to determine the presence or the absence of an effect of acceleration of follicle growth caused by said other compound.
 - 13. Use of a somatostatin antagonist analogue for preparing a medicament intended to accelerate the start of growth of the quiescent follicles in non-menopausal women.
- 14. Use according to claim 13, characterized in that the somatostatin antagonist analogue is chosen from the peptides of general formula (III)

$$A^1$$
-cyclo {D-Cys- A^2 -D-Trp- A^3 - A^4 -Cys}- A^5 -Y¹
(III)

in which:

5

10

 A^1 is an optionally substituted aromatic α -amino acid;

 A^2 is an optionally substituted aromatic α -amino acid;

A³ is Dab, Dap, Lys or Orn;

 A^4 is β -Hydroxyvaline, Ser, Hser, or Thr;

 A^5 is an optionally substituted aromatic D- or L- α -amino acid; and

Y¹ is OH, NH₂ or NHR¹, R¹ being (C₁₋₆)alkyl;

such methyl group in a peptide of general formula (III);

each optionally substituted aromatic α-amino acid being optionally substituted with one or more substituents independently chosen from the group comprising a halogen atom and the groups NO₂, OH, CN, (C₁₋₆)alkyl, (C₂₋₆)alkenyl, (C₂₋₆)alkynyl, (C₁₋₆)alkoxy, Bzl, O-Bzl and NR⁹R¹⁰, R⁹ and R¹⁰ each being independently H, O, or (C₁₋₆) alkyl; and each nitrogen atom with a peptide amide bond and the amino group of A¹ being optionally substituted with a methyl group, it being understood that there is at least one

and the pharmaceutically acceptable salts and protected forms of such peptides.

- 15. Use according to claim 13, characterized in that the somatostatin antagonist analogue is chosen from the group comprising:

- Cpa-cyclo[D-Cys-Pal-D-Trp-N-Me-Lys-Thr-Cys]-D-Trp-NH₂;
- Cpa-cyclo[D-Cys-Tyr-D-Trp- N-Me-Lys-Thr-Cys]-Nal-NH₂;
- Cpa-cyclo[D-Cys-Pal-D-Trp- N-Me-Lys-Thr-Cys]-Nal-NH₂;
- the peptide known by the code name AC-178,335;
- the octapeptide known by the code name ODN-8;
 - the peptide known by the code name SB-710411;
 - * the peptide known by the code name BIM-23056;
 - the compound known by the code name BN-81674;
 - the compound known by the code name SRA-880;

15

- and their pharmaceutically acceptable salts and protected forms.
 - **16.** Use of a somatostatin antagonist analogue in order to support *in vitro* follicle development.
 - 17. Use of a somatostatin antagonist analogue in toxicology tests relating to another compound in order to determine the presence or the absence of an effect of slowing the follicle growth caused by said other compound.